DETAILED ACTION

Group H, claims 61, 73-77, a method for diagnosis of colon cancer, by detecting the level of the nucleic acid of SEQ ID NO:59 are examined in the instant application.

The embodiment of claims 73-76 as drawn to a method for detecting predisposition to colon cancer have been withdrawn from consideration as being directed to a non-elected invention.

Withdrawn Rejection

The 112, second paragraph is withdrawn in view of the amendment.

Claim Rejections - 35 USC § 112, First Paragraph, Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 61, 73-77 remain rejected under 35 U.S.C. 112, first paragraph, for lack of enablement for a method for detecting colon cancer, for reasons already of record in paper of 12/23/08.

1. Diagnosis of colon cancer.

The response asserts as follows:

The Office Action alleges that it is not clear if non-cancerous colon tissue was used in the specification. Applicants respectfully submit that the adequacy of the disclosure is judged from

the perspective of one of ordinary skill in the art and that the skilled person would understand that a "normal control" refers to healthy tissue of the corresponding organ. "[a] patent need not teach, and preferably omits, what is well known in the art." Spectra-Physics, Inc. v. Coherent, Inc., 827 F.2d 1524, 1534 (Fed. Cir. 1987).

The Office Action cites Stanton et al., British J. Cancer 70:427 (1994), Iehle et al., J. Steroid Biochem. Mol. Biol. 68:189 (1999) and Abbaszadegan et al., Cancer Res. 54:4676 (1994) for the proposition that the expression level of a nucleic acid in cancer is not predictable. None of the cited references discuss currently claimed SEQ ID NO:59, which is disclosed in the specification as being differentially expressed in cancer. Accordingly, it respectfully submitted that these references are not relevant to the specifically recited nucleic acid of the claimed invention and the enablement of the invention.

The Office Action alleges that a difference encompasses an increase and a decrease and asserts it is unpredictable which one, increase or decrease, is predictive of colon cancer. It is respectfully submitted that the specification discloses that SEQ ID NO: 59 is differentially expressed in colon cancer. It would be routine for the skilled person to measure the expression level of SEQ ID NO:59 in colon cancer and normal control tissue to confirm the differential expression and determine which tissue has increased expression vis-a-vis the other. The Examiner is respectfully reminded that the mere fact that the experimentation may have been difficult and time consuming does not mandate a conclusion that such experimentation would have been considered to be 'undue' in this art. Indeed, great expenditures of time and effort were ordinary in the field of cancer therapies and diagnostics.

The response has been considered but is not found to be persuasive for the following reasons:

The specification discloses that the cDNA sequence is screened for differential expression in cancer, using human colon cancer tissue and normal tissue (Example 3 on page 138 and Example 4 on page 142). However, the specification does not have any actual data supporting such assertion. In the absence of objective evidence, one cannot predict that SEQ ID NO:59 is differentially expressed in colon cancer tissue as compared to non-cancerous colon tissue, because it is well known in the art that the level of expression of a nucleic acid in a cancer tissue is not predictable, in view of the teaching of Stanton et al, Iehle et al, and Abbaszadegan et al, all of record. Although Stanton et al, Iehle et al, and Abbaszadegan et al do not specifically recite the claimed nucleic acid of SEQ ID NO:59, the teaching of Stanton et al, Iehle et al, and Abbaszadegan et al applies as well to the claimed nucleic acid of SEQ ID NO:59.

Further, in view of a lack of a definition of normal tissue or normal control or non-cancerous control in the specification, any tissue, which does not have to be non-cancerous colon cancer, could be used. The level of SEQ ID NO:59 is such tissue as compared to non-cancerous colon tissue is not predictable.

Further, screening assays to determine which one of claimed differential expression of SEQ ID NO:59, i.e., an increase or a decrease, in colon cancer tissue as compared to non-cancerous colon tissue, do not enable the claimed invention. The court found in *Rochester v. Searle*, 358 F.3d 916, Fed Cir, 2004, that screening assays, and by inference suggestions of structural analysis, are not sufficient to enable an invention because they are merely a wish or plan for obtaining the claimed chemical invention.

In addition, the claimed method, as claimed in claim 77, would be non-specific, because a **complement** could be a full or partial complement, wherein the partial complement of SEQ ID NO:59 needs to share with SEQ ID NO:59 only a few complementary nucleotides.

2. Claims 73-76 also remain rejected under 112, first paragraph, for lack of enablement for a method for diagnosis of colon cancer, using a sequence **at least 95% or 98% identical to SEQ ID NO:59**, in view of the teaching of Schmid et al and Conner et al, all of record.

Rejection remains because the response does not answer to this issue.

New Rejection due to the Amendment

Claim Rejections - 35 USC § 112, First Paragraph, Enablement

Claims 73-76 are rejected under 35 U.S.C. 112, first paragraph, for lack of enablement for a method for detecting colon cancer, using breast or prostate tissue sample.

Claims 73-76 encompass a method for detecting colon cancer, by detecting the level of SEQ ID NO:59 or 95% variant thereof in breast or prostate tissue, to which colon cancer cells have **metastasized**.

The specification discloses that cDNA sequences are screened for differential expression in cancer, using tumor tissue sample, including human colon cancer tissue and normal tissue, including non-cancerous prostate sample (Example 3 on page 138, Example 4 on page 142).

The specification does not have any data or objective evidence that SEQ ID NO:59 is differentially expressed in colon cancer, when using breast or prostate cancer tissue as a test sample.

It is unpredictable that metastasized cancer cells still express the claimed sequences,

because expression of a sequence could be lost during the progression toward metastasis. For example, Kibel, AS et al, 2000, J urol, 164(1): 192-6 teach that gene expression in the chromosomal region 12p12-13 is different in primary and metastatic prostate cancer cells, and that inactivation in the chromosome region 12p12-13 occurs prior to metastasis. Similarly, Dong et al, 2000, Cancer Research, 60: 3880-3883, teach that deletion of a region in the chromosome 13q21 is associated with aggressive prostate cancer, as compared to less aggressive prostate cancer, such as primary prostate cancers that are not yet differentiated (abstract, and figure 1 on page 3882). Russo, V et al, 1995, Int J Cancer, 64: 216-221, teach that analysis of multiple metastatic lesions and primary breast tumors show that in some cases the MAGE gene expression is lost during metastasis, but in some other cases, in metastasis nodes derived from MAGE-negative primary tumors, MAGE gene expression is detected (abstract, and table II on page 220). Thus in view of the above, one cannot predict that the claimed sequences are useful for diagnosis of the presence in a subject of an invasive colon tumor.

MPEP 2164.03 teaches that "the amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability of the art. In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The amount of guidance or direction refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature ot the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is

unpredictable, the specification would need more detail as how to make and use the invention in order to be enabling."

Given the above unpredictability, and in view of the complex nature of the invention, a lack of sufficient disclosure in the specification, and little is known in the art concerning the claimed invention, there would be an undue quantity of experimentation required for one of skill in the art to practice the claimed invention, that is commensurate in scope of the claims.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINH-TAM DAVIS whose telephone number is 571-272-0830. The examiner can normally be reached on 9:00 AM-5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, LARRY HELMS can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

MINH-TAM DAVIS
October 21, 2009

/Larry R. Helms/

Supervisory Patent Examiner, Art Unit 1643